

A2 two potential N-glycosylation sites as well as the cysteines capable of forming a disulfide bond are shown underlined and in bold font.

Please delete the paragraph on page 1, lines 21-22, and replace it with the following paragraph:

A3 Fig. 4 is a protein alignment comparing human interferon-beta-2 (SEQ ID NO: 16) to other interferon types (SEQ ID NOS 17-30).

Please delete the paragraph on page 2, line 5, and replace it with the following paragraph:

A4 Fig. 12 is a 5' genomic nucleotide sequence (residues 1-394 of SEQ ID NO: 15) of human IFN- $\beta$ 2.

Please delete the paragraph on page 2, line 6, and replace it with the following paragraph:

A5 Fig. 13 is a nucleotide sequence (residues 395-648 of SEQ ID NO: 15) coding for a 5' region of human IFN- $\beta$ 2.

Please delete the paragraph on page 2, line 7, and replace it with the following paragraph:

A6 Fig. 14 is a 5' polypeptide sequence (residues 1-69 of SEQ ID NO: 16) of human IFN- $\beta$ 2.

Please delete the paragraph on page 5, lines 1-24, and replace it with the following paragraph:

A7 Other homologs of IFN- $\beta$ 2's of the present invention can be obtained from mammalian and non-mammalian sources according to various methods. For example, hybridization with oligonucleotides (e.g., primers to amplify the coding region -5' ATG ATT ATC AAG CAC TTC TTT GGA-3' (SEQ ID NO: 1) and 5'-CTA CCT CGG GCT TCT AAA CTC TGT-3' (SEQ ID NO: 2)). Primers used for expression in E. coli - 5'GGA ATT CCT ACT ACC TCG GGC TTC TAA-3' (SEQ ID NO: 3) and 5'-GCG CGC GCATAT GCT AGA TTT GAA ACT GAT TAT-3' (SEQ ID NO: 4). Primers for the full length known sequence including 5' and 3' untranslated

Q7 genomic sequence -5'-TTT AGG TGA CAC TAT AGA AT-3' (SEQ ID NO: 5) and 5'-TAA AAT GGA TAG AAT ATA TAA-3' (SEQ ID NO: 6) - can be employed to select homologs, e.g., as described in Sambrook et al., Molecular Cloning, Chapter 11, 1989. Such homologs can have varying amounts of nucleotide and amino acid sequence identity and similarity to IFN- $\beta$ 2. Mammalian organisms include, e.g., rodent, mouse, rat, hamster, monkey, ape, pig, cow, horse, dog, cat, etc. Non-mammalian organisms include, e.g., vertebrates, invertebrates, zebra fish, chicken, Drosophila, C. elegans, Xenopus, yeast such as S. pombe, S. cerevisiae, roundworms, prokaryotes, plants, Arabidopsis, Crustacea, artemia, viruses, etc. To select oligonucleotides for hybridization an effective method can be used. For example, IFN- $\beta$ 2-specific regions can be identified by comparing and IFN-B-2 of the present invention with other IFN- $\beta$ 2 types and selecting those amino acid sequences which only appear in the former (i.e., non-conserved, or, "specific-for" IFN- $\beta$ 2). See Fig.4 showing conserved and non-conserved regions between the different interferon types. Non-conserved amino acid sequences can be chosen (e.g., KSLSP (SEQ ID NO: 9)) and degenerate probes can be designed based on such sequences. See, also, Venkataraman et al., Proc. Natl. Acad. Sci., 96:3658-3663, 1999. Other specific (i.e., non-conserved) and/or conserved amino acid sequences can be found routinely e.g., by searching a gene/protein database using the BLAST set of computer programs.

---

Please delete the paragraph on page 5, lines 25-31 thru page 6, lines 1-3, and replace it with the following paragraph:

---

Q8 The invention also relates to IFN- $\beta$ 2-specific amino acid sequences, e.g., a defined amino acid sequence which is found in the particular sequence of Figs. 2 and 4, but not in other interferon types. Preferred polypeptides are at least about eight contiguous amino acids, e.g., about 9, 10, 12, 15, 20, 21, 22, 25, 30, 40, 50, etc. Such polypeptides can comprise, e.g., KHFFGTV (SEQ ID NO: 7), IIFQQRQV (SEQ ID NO: 8), KSLSP (SEQ ID NO: 9), FRANI (SEQ ID NO: 10), AEKLSGT (SEQ ID NO: 11), CLFFVFS (SEQ ID NO: 12), QGRPLNDMKQELTTEFRSPR (SEQ ID NO: 13), and fragments thereof. An

Q8 IFN- $\beta$ 2-specific amino acid sequence or motif can be useful to produce peptides as antigens to generate an immune response specific for it. Antibodies obtained by such immunization can be used as a specific probe for a mammalian IFN- $\beta$ 2 protein for diagnostic or research purposes, including as expression markers.

Please delete the paragraph on page 16, lines 25-31 thru page 7, lines 1-12, and replace it with the following paragraph:

Q9 Another aspect of the present invention is a nucleotide sequence which is unique to a mammalian IFN- $\beta$ 2. By a unique sequence to an IFN- $\beta$ 2, it is meant a defined order of nucleotides which occurs in IFN- $\beta$ 2, e.g., in the nucleotide sequences of Fig 1, but rarely or infrequently in other nucleic acids, especially not in an animal nucleic acid, preferably mammal, such as human, rat, mouse, etc. Unique nucleotide sequences include the sequences, or complements thereto, coding for amino acids KHFFGTV (SEQ ID NO: 7), IIFQQRQV (SEQ ID NO: 8), KSLSP (SEQ ID NO: 9), FRANI (SEQ ID NO: 10), AEKLSGT (SEQ ID NO: 11), CLFFVFS (SEQ ID NO: 12), QGRPLNDMKQELTTEFRSPR (SEQ ID NO: 13), and fragments thereof as shown in Fig. 1. Such sequences can be used as probes in any of the methods described herein or incorporated by reference. Both sense and antisense nucleotide sequences are included. A unique acid according to the present invention can be determined routinely. A nucleic acid comprising such a unique sequence can be used as a hybridization probe to identify the presence of, e.g., human or mouse IFN- $\beta$ 2, in a sample comprising a mixture of nucleic acids, e.g., on a Northern blot. Hybridization can be preformed under high stringent conditions (see above) to select nucleic acids (and their complements which can contain the coding sequence) having at least 95% identity (i.e., complementarity) to the probe, but less stringent conditions can also be used. A unique IFN- $\beta$ 2 nucleotide sequence can also be fused in-frame, at either its 5' or 3' end, to various nucleotide sequences as mentioned throughout the patent, including coding sequences for other parts of IFN- $\beta$ 2, enzymes, GFP, etc, expression control sequences, etc.